Comparison of Growth in Infants according to Maternal HIV-status in Harare, Zimbabwe

A student thesis by Veronica Martinsen & Sanpreet Kaur Grewal

V-08

Supervisors:

Dr. Nyaradzai Edith Kurewa, Harare, Zimbabwe

&

Prof. Dr. Med Babill Stray-Pedersen, Oslo

TABLE OF CONTENTS

ABSTRACT

Background: Sub-Saharan Africa is representing 69 % of the global HIV burden, with an estimated number of 34 million HIV positive people worldwide, 1.2 million HIV positives are living in Zimbabwe. With around one in seven adults living with HIV today, Zimbabwe is experiencing one of the most severe HIV/AIDS epidemics in the world. In 2010, more than 13 % of the population in Zimbabwe was younger than 5 years, and according to UNICEF, as many as one in four children in Zimbabwe are orphaned as a result of parents dying from HIV/AIDS.

We wanted to study the growth among a group of infants related to maternal HIV-status in the Harare region during 2002-2003 related to the WHO growth charts.

Method: Our study is based on a broader prospective cohort study about mother to child transmission (MTCT) of HIV in Harare, lasting from April 2002 to November 2003. A total of 1050 pregnant women were enrolled at gestational age 36 from three clinics outside Harare. 774 (408 HIV negative mothers and 366 HIV positive mothers) met our criteria of inclusion. They were followed up with their index child, and measurements of weight, length and head circumference were taken at birth, 6 weeks, 4 months and 9 months of age. Data on boys and girls were analysed separately. The sample size for the boys and girls who had their measurements registered at all time points were 122 and 122 for weight, 116 and 122 for length, and 120 and 124 for head circumference respectively.

Results:. The differences we found in growth according to maternal HIV-status at the different time points, were of no statistical significance ($p>0.05$). Neither did we find any significant differences in low birth weight (< 2500 g) in the two groups We also compared the growth curves to WHO´s growth standards, to see how many of the children who fell beneath the 3^{rd} percentile and above the 97^{th} percentile. We found that the mean for length lies lower and the mean for head circumference lies higher for the infants in the study, in comparison to the WHO growth standards.

According to maternal HIV-status, we found that there were almost fifteen times more deceased mothers and more than three times more deceased infants in the HIV-positive group. Amittedly, all the children who died before 9 months of age are not included in our

growth analysis, and may have influenced the results in the HIV positive group in a negative favour.

Conclusion: In our study results we found no differences in growth of statistical significance according to maternal HIV-status the first 9 months of life. What we did find, was that HIV positive mothers had a higher mortality and so did their children.
The findings in our study might be unreliable due to several possible sources of bias, with measurement errors being one of these. Since it is likely to believe that these errors were equally divided in both groups, we still believe that our results are to be considered as valuable. Similar studies in other African countries show variable results, and further research is needed to conclude that there is no difference in growth according to maternal HIV-status.

ACRONYMS

AIDS: Acquired Immunodeficiency Syndrome
ANC: Antenatal Care
ART: Anti-retroviral therapy
ARV: Antiretroviral
BHAMC: Better Health for African Mother and Child
CDC: The Centers for Disease Control and Prevention
HDI: Human Development Index
HIV: Human Immunodeficiency Virus
MGRS: Multicentre Growth Reference Study
MTCT: Mother To Child Transmission
PEPFAR: US President´s Emergency Plan for AIDS Relief
PMTCT: Prevention of Mother To Child Transmission
STI: Sexually Transmitted Infections
UNICEF: United Nations International Children´s Emergency Fund
USD: United States Dollar
WHO: World Health Organization
ZANU: Zimbabwe African National Union

1.0 INTRODUCTION

1.1 Problem statement

The HIV pandemic has been and is still a big global health challenge. Zimbabwe has been one of the most affected countries, which is why we wanted
to do our project there. When choosing the topic for our thesis, we wanted to focus on HIV and child health because of its impact on the global future. Three of the United Nations Millennium Development Goals are related to this: reduce child mortality, improve maternal health and combat HIV/AIDS. (1)

The topic we chose within HIV and child health was infant growth. We wanted to learn if there were any differences in growth patterns in infants born by HIV-positive mothers compared to infants born by HIV-negative mothers in Harare, with focus on development in weight, length and head circumference. In relation to that we also wanted to see how other factors were divided in the two groups, like breastfeeding patterns, because of its big impact on child growth.

1.2 About Zimbabwe

The Republic of Zimbabwe is landlocked in the south-east of Africa, bounded by South Africa in the south, Botswana in the south-west, Zambia in the north-west and Mozambique in the north and the east. (2) It is the 59th largest country in the world, a below-average size for Africa, and covers 390 580 square kilometres. It lies on an extensive inland plateau 900 meters or more above sea level. (3)

Zimbabwe is a country with many resources, including minerals and a good climate for varied agriculture. Tobacco, gold and cotton have been the most important export products. Other important productions are corn, wheat, sugar, peanuts, soybeans, tea, coffee, meat, fish, flowers, fruits and vegetables. The political unrest has unfortunately had a negative impact on the tourist industry. (4)

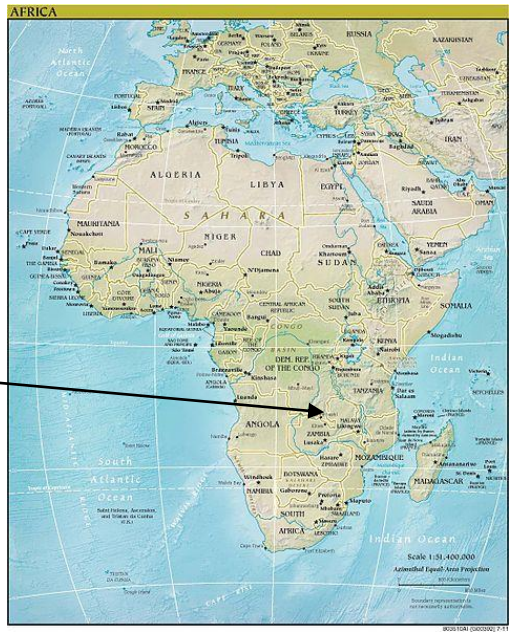
According to WHO, the estimated total population in Zimbabwe in 2010 was 12 571 000. (5) Other numbers from 2010 are: population under 18 years: 5 866 000 and population under 5

years: 1 692 000. (6) From these statistics, 46.7 % of the total population was younger than 18 years old and 13.5 % younger than 5 years old.

The HDI for Zimbabwe has fallen from a rank of 130th in 1999 to 151th in 2007 out of 177 countries (7), and was in 2011 ranked number 173 out of 187 countries. (8)

Figure 1: Map of Zimbabwe

Figure 2: Map of Africa



1.3 Zimbabwe and healthcare

Throughout Zimbabwe´s 10 provinces, there are 126 mission hospitals and clinics. There have been an increasing number of patients from Harare to the rural mission hospitals after the closure of public hospitals in Harare in 2008. (7)

The new State of Zimbabwe became legally independent in April 1980, the same year as Robert Mugabe became Prime Minister (later President) and leader of the ZANU-PF government. (3) The government's actions have markedly worsened the collapse of the healthcare system. The lives of most Zimbabweans improved dramatically in the first years of independence, due to significant economic and social progress. The healthcare system in Zimbabwe was so good in the 1990s that 85 % of the population lived within 10 km of a health facility. (7) Unfortunately, due to Mugabe´s economic policies, the 1990s featured a number of strikes, and in 1997 a national strike paralyzed the country. (3)

Zimbabwe experienced an economic collapse, which again led to a sharp rise in unemployment, food insecurity and malnutrition because of a dramatically fall in agricultural production, destruction of the public healthcare and outbreaks of infectious diseases. The public health system collapse hit the public hospitals and clinics, the most basic state functions in protecting the health of the population. As late as in 2008, there were no intensive care unit and no functioning critical care beds in the public sector. Most wards and surgical suits gradually closed, and paediatric surgeries ceased between September and November 2008. The closure of hospitals also affected the medical students, and for a period the medical school closed. Private sector user fees for medical services were way more expensive than the majority of the population could afford: 3000 USD for a Caesarean section, 500 USD to secure a bed and 200 USD in cash for a medical consultation. As a consequence of this, the whole population but the wealthiest Zimbabweans were denied access to medical help. (7)

The crisis also led to a collapse in the water delivery systems, contamination of surface water, loss of water supply through leakage from broken water pipes and clogged sewerage pipes leading to non-functional toilets. To manipulate elections, the Mugabe government established severe food restrictions during election periods from 2000 persisting until 2008. In 2008, all actions of charitable organizations were stopped, and international humanitarian organizations were prevented from delivering food aid. The food insecurity also had an impact on the HIV/AIDS epidemic, with an increase in commercial sex. Many women considered prostitution to be the last and best opportunity to earn money to buy food to their families. The HIV-infected part of the population were especially vulnerable to the food and water crisis, because of their impaired immune system and increased risk of other infections, weight loss and diarrhoea. (7)

The diminished access to care, public hospital closings and inadequate or unaffordable medical supplies, led to a drastic fall in vital statistics; including increased maternal, adult and infant mortality, cholera epidemics, and worsening of HIV/AIDS, tuberculosis, malnutrition and vitamin deficiency. (7)
The life expectancy at birth also fell dramatically. Life expectancy at birth (mean age both sexes): 55 years (1970), 61 years (1990), 36 years (2006), 50 years (2010). (6)

In addition, there has been lack of access to essential medications and medical supplies, including the access to HIV/AIDS care and treatment. Since 2006, different HIV/AIDS donor programs like the PEPFAR program, the Global Fund to Fight AIDS, Tuberculosis and

Malaria and the CDC, have been affected by the same political control, which has affected the healthcare in Zimbabwe. (7)

1.4 Zimbabwe and HIV

Zimbabwe has had severe HIV/AIDS and tuberculosis epidemics for more than two decades. In 1999, UNAIDS considered Zimbabwe to be the highest prevalence country for HIV infection worldwide, with one in four of all adults HIV positive. (7)
The most detrimental effect on Zimbabwe´s dwindling population has probably been the prevalence of HIV/AIDS. With around one in seven adults living with HIV today, Zimbabwe is experiencing one of the most severe HIV/AIDS epidemics in the world. (3)

According to UNAIDS World AIDS Day Report (2012), an estimated number of 34 million people are HIV positive globally. The majority of new HIV infections occur in Sub-Saharan Africa, and counts for 23.5 million of the total number. In other words, Sub-Saharan Africa is representing 69 % of the global HIV burden. Out of these, 1.2 million are living in Zimbabwe. Most countries in Southern Africa have a high HIV prevalence, but the incidence has been dramatically reduced the last decade. Between 2001 and 2011, the rate of new HIV infections among adults (15-49 years) dropped by 50 % in Zimbabwe. Between 2005 and 2011, Sub-Saharan Africa has cut the number of people dying of AIDS-related causes by 32 %, nearly 90 000 fewer deaths in Zimbabwe. (9)

The notable decline in HIV prevalence has been attributed to both high mortality and a decline in HIV incidence. (10) The decline in HIV incidence is a result of safer sexual behaviours (including increased condom use, reduced number of sexual partners, later sexual debut and more information about HIV), and an increasing number of people accessing treatment with ARV drugs. In some countries though, the prevalence has increased instead of stabilizing or declining, due to increased survival of infected people due to treatment. (11) In 2004, the U.S. funded PEPFAR program began providing support for ART. Before 2004, HIV/AIDS treatment was largely unavailable in Zimbabwe. (7) According to CDC, the reported number of people receiving ART in Zimbabwe in February 2010, was 218 589. The estimated number of people needing ART was 640 000. (12)

Zimbabwe has an enormous number of AIDS orphans, children who have lost one or both parents to AIDS. Zimbabwe has a higher percentage of orphans than any other country in the world. According to UNICEF, as many as one in four children in Zimbabwe are orphaned as a result of parents dying from HIV/AIDS. (3)

Estimated number of children who have lost their mother, father or both parents to AIDS, and who were alive and under age 17: 720 000 (2001). (13)

Estimated number of children and adults living with HIV. (25)

Population	**2001**	**2002**	**2003**
Estimated children (0-14)	210 000	220 000	230 000
Estimated adults (15+)	1 600 000	1 500 000	1 400 000
Estimated women (15+)	880 000	850 000	800 000

Estimated HIV prevalence (%) among adults (age 15-49) in 2001 was 26%, however in the last decade the prevalence has decreased to almost the half. (6), (13)

1.5 Paediatric HIV and mother-to-child transmission

In 2011, 330 000 infants were newly infected with HIV globally, a 43% decline since 2003 and 24% decline since 2009. The primary cause of this reduction is the focus on ARV- and infant feeding-based prevention services. Coverage of effective ARV regimens for preventing MTCT of HIV, reached 57% in low- and middle-income countries the same year. Even though access to treatment and care in developing countries are expanding, only 28% of children in need received ART in 2011, compared to 58% for adults. (14)

Transmission rate for HIV has been reported to range from 14% to 64%, with a higher rate in Africa compared to Europe and North America. This reflects a higher prevalence of risk factors in African women. (15) More than 95% of HIV infected children acquired the virus due to vertical transmission. In absence of ART, the transmission rate varies from 20% to 30%. Vertical transmission can happen at any time during the perinatal period from early gestation, delivery and postnatal period through breastfeeding. When it comes to the perinatal transmission, most (50% to 80%) are believed to occur near or during delivery. (16)

Risk factors for MTCT can be divided into maternal and obstetric:

1. *Maternal risk factors:* , increased viral load, anaemia, low maternal CD4+ lymphocyte count, frequency of intercourse during pregnancy, multiple sexual partners, and presence of other sexually transmitted diseases, cigarette smoking and illicit drug use (17)
2. *Obstetric risk factors:* prolonged rupture of amniotic membranes, mode of delivery (elective C-section as protective), birth order in twin gestation, placental disruption or inflammation and obstetric complications. (17)

1.6 Growth in infants

The extra uterine growth happens in three stages: infancy, childhood and puberty. Infancy growth begins with a rapid growth, especially seen on the weight curves. Children with growth retardations at delivery, have a catch-up-growth the first months. After the first year of living, the growth seems to slow down. The biggest influence on growth the first year of life is the infant's nutritional status, while growth hormones have less impact. A child with lack of growth hormone can have an almost normal growth chart in this period. (18)

The term failure to thrive is commonly used for children who grow less than expected over a time period. The ethology can be multifactorial, with chronic infection being one of the possible causes along with other psychosocial, environmental, nutritional, endocrine and metabolic factors. (18)

Changes in height, weight, and head circumference are used as indicators for normal and pathologic growth. These are compared with established standards for a given population at a given age in a growth chart. When evaluating a child's growth, one must consider its genetic potential. Growth velocity, the change in growth over time, is a more sensitive index of growth than a single measurement. (19)

When comparing growth in the infants in our study, we have used WHOs child growth standards for growth velocity, based on weight, length and head circumference. These standards are made after the WHO MGRS from 1997 to 2003 in USA, Oman, Norway, Brazil, Ghana and India. A total of 1737 children (894 boys and 843 girls) were followed from birth to 24 months in a longitudinal study component in the MGRS. (20)

1.7 WHO guidelines on HIV and infant feeding

The newest WHO guidelines on HIV and infant feeding are from 2010. Principles used making these guidelines include not only reducing MTCT of HIV, but also balancing HIV prevention with other causes of child morbidity and mortality, while meeting the nutritional requirements. The focus is thus now on securing a HIV free survival of the child. Every nation should decide which of these two strategies to use: (21)

1. Breastfeed and receive full ARV intervention.
2. Avoid all breastfeeding (most likely to give the child an HIV-free survival).

Decision should be made considering the socio-economic and cultural contexts, availability and quality of health services, local epidemiology and main cause of maternal and child undernutrition and infant and child mortality. In many of the developing countries, the most important causes of child morbidity and mortality are malnutrition and other diseases such as diarrhoea. (21)

When the national strategy is breastfeeding and full ARV intervention, recommendations are following: (21)

- Mothers known to be HIV-infected should exclusively breastfeed the first six months, and thereafter introduce appropriate complementary foods while continuing breastfeeding the twelve first months of life.
- Breastfeeding should only stop once a nutritionally adequate and safe diet without breast milk can be provided.

And what happens when this strategy is chosen, but ARVs are unavailable? (21)

- Even in these conditions mothers should be counselled to exclusively breastfeed in the first six months of life and continue breastfeeding thereafter, unless environmental and social circumstances are safe for, and supportive of, replacement feeding.

2.0 METHOD

BHAMC is the name of a project started in 2002, as a study of national PMTCT of HIV and other STIs. The project is a cooperation between Universities in Zimbabwe, Tanzania and Norway. (26)

A standardised questionnaire to determine demographic, socioeconomic, obstetric history, sexual behaviour and life styles was used in an interview with all the women participating. Biological samples were collected to screen for STIs, including HIV infection. Infant anthropometrical measurements were taken at each scheduled visit (birth, 6 weeks, 4 months and 9 months). (27) Weight-for-length charts are commonly used in paediatrics, but because of uncertain measurements of length of the infants in our study, we chose to use the single measurements of weight and length.

2.1 Study area and population

This study took place in Harare, the capital city of Zimbabwe. Harare is geographically placed in Mashonaland, north-east in Zimbabwe, and has a population of approximately 1.6 million (in 2006). Zimbabwe's largest ethnic group, the Shona people, have their cultural centre in the capital. (22)

Three peri urban clinics were included in the study: St. Marys Clinic, Seke North Makoni and Epworth. These clinics offer maternal and child health services. St. Marys Clinic and Seke North Makoni fall under Chitungwiza municipality, approximately 30 km south of Harare, with a population of 321 782 in 2002 (23). Chitungwiza was earlier a part of Harare, but is now an independent city. (22) Epworth lies in a peri urban residential area called Mashonaland East Province, situated 12 km south-east of Harare, with a population of 1.1 million in 2002 (24). A total of 1050 pregnant women were enrolled from these three clinics, and were followed with their newborns after delivery.

2.2 Study design

Our study is using data from the BHAMC: a prospective cohort study about MTCT of HIV in Harare, lasting from April 2002 to November 2003. HIV positive and negative pregnant

women were enrolled at gestational week 36, after being pre- and post-test counselled for HIV infection as part of the National program on PMTCT. (27) Mothers and their infants were initially followed up from birth, 6 weeks, 4 months and 9 months of age, and every 6 months thereafter until 5 years of age.

In August 2011, we spent four weeks in Harare to collect the material from this study for our project. The data was already sorted in individual files for each couple of mother and child, a total of 1050 files. We went through data from all of these files and used follow-up information about the mother and the children until 9 months of age.

2.3 Criteria for inclusion

To be included, these criteria had to be recorded:

1. HIV status of the mother
2. HIV status of the infant
3. Weight, length and head circumference at birth of the infant
4. Gender of the infant

We went through 1050 files in total, and out of these, 774 (408 HIV negative mothers and 366 HIV positive mothers) met our criteria of inclusion. The variables we chose to use and collect were following:

1. Age mother
2. Education level
3. Marital status
4. HIV-status of mother
5. HIV-status of infant
6. Gender of infant
7. Weight, length and head circumference at birth, 6 weeks, 4 months and 9 months of age
8. Deceased mothers
9. Deceased infants
10. Breastfeeding or not
11. Summary of clinic visits with infant after birth

2.4 Data analysis plan

We looked at girls and boys separately, because of the known differences in growth between them, with boys having a higher weight, length and head circumference in general. When analysing, we first found the mean values for weight, length and head circumference at birth, 6 weeks, 4 months and 9 months for all registered data. Then we did the same, but only of those children who had their recordings at all the time points for each parameter, meaning that they for example had to have their weight registered at birth, 6 weeks, 4 months and 9 months. Therefore we missed out the deceased children; one stillbirth, two died before 6 weeks, 14 before 4 months and 29 before 9 months of age. This gave us a selected group, and the groups were different for weight, length and head circumference. In both of these study groups, we found no difference in mean values for growth that was of statistically significance, between children of HIV negative and HIV positive mothers. In our results, we have therefor decided to use the analyses from our selected study group.

Our statistical analysis were done using SPSS statistical software version 20.0 for Macintosh. An independent-samples t-test was used to compare growth means between children of HIV negative and HIV positive mothers. The significance level was set to $p < 0,05$ and a 95% confidence interval was used to measure the strength of association between a potential effect. We also used SPSS to do frequency tests, crosstabs and chi-square test for other factors such as maternal age, education level, marital status, breastfeeding, infant follow up visits and deceased mothers and infants, to see if there were any differences according to maternal HIV-status.

Growth curves for comparing growth in the two groups and to WHO growth standards, were made using Microsoft Excel for Mac 2011, version 14.2.4.

2.5 Ethical clearance

The Medical Research Council of Zimbabwe and the Ethical Committee in Norway have given the ethical clearance for BHAMC.

3.0 RESULTS

The records of children born to 774 mothers (408 HIV negative and 366 HIV positive) were investigated. Only children where the growth parameters were recorded during the first 9 months of life were included.

Analyses were done separately for boys and girls. The number of boys and girls who had their weight registered at all time points were 122 and 122 respectively (table 1), for length 116 and 122 respectively (table 2) and for head circumference 120 and 124 respectively (table 3).

3.1 Weight

Table 1: Weight of boys and girls according to maternal HIV-status

		Maternal HIV status	N	Mean weight (kg)	SD	p-value	95% CI lower	95% CI upper
BOYS	**Birth**	Neg	52	3,14	0,38	0,27	-0,07	0,25
		Pos	70	3,05	0,48			
	6 weeks	Neg	52	4,90	0,61	0,14	-0,07	0,44
		Pos	70	4,71	0,80			
	4 months	Neg	52	7,49	1,14	0,39	-0,26	0,66
		Pos	70	7,29	1,34			
	9 months	Neg	52	9,09	1,55	0,71	-0,46	0,68
		Pos	70	8,98	1,58			
GIRLS	**Birth**	Neg	59	3,04	0,36	0,86	-0,14	0,17
		Pos	63	3,03	0,50			
	6 weeks	Neg	59	4,49	0,66	0,70	-0,18	0,27
		Pos	63	4,45	0,61			
	4 months	Neg	59	6,74	1,30	0,58	-0,33	0,58
		Pos	63	6,61	1,24			
	9 months	Neg	59	8,51	1,39	0,46	-0,33	0,71
		Pos	63	8,32	1,50			

Table 1 shows that the boys and girls born of HIV negative mothers (n = 52, n = 59) had a tendency to higher mean weight at all time points, compared to those born of HIV positive mothers (n = 70, n = 63), but not statistically significant (p > 0,05). As expected the boys had å higher mean weight at all time points.

3.2 Length

Table 2: Length of boys and girls according to maternal HIV-status

		Maternal HIV status	N	Mean length (cm)	SD	p-value	95% CI lower	95% CI upper
BOYS	**Birth**	Neg	50	49,5	2,59	0,22	-0,45	1,99
		Pos	66	48,7	3,72			
	6 weeks	Neg	50	54,2	5,35	0,19	-3,10	0,63
		Pos	66	55,4	4,76			
	4 months	Neg	50	62,3	4,69	0,26	-0,78	2,83
		Pos	66	61,3	4,99			
	9 months	Neg	50	68,5	5,65	0,77	-2,32	1,72
		Pos	66	68,8	5,27			
GIRLS	**Birth**	Neg	60	48,7	2,62	0,11	-0,21	2,06
		Pos	62	47,7	3,62			
	6 weeks	Neg	60	54,8	3,51	0,66	-1,19	1,87
		Pos	62	54,4	4,90			
	4 months	Neg	60	60,7	5,08	0,99	-1,90	1,88
		Pos	62	60,7	5,46			
	9 months	Neg	60	67,5	5,00	0,05	-0,01	4,09
		Pos	62	65,5	6,35			

Table 2 shows that the boys born of HIV negative mothers (n = 50) had a tendency to higher mean length at birth and 4 months, while boys born of HIV positive mothers (n = 66) had tendency to higher mean length at 6 weeks and 9 months. The girls born of HIV negative mothers (n = 60) had tendency to higher mean length at birth, 6 weeks and 9 months. None of these differences however, were statistically significant (p > 0,05).

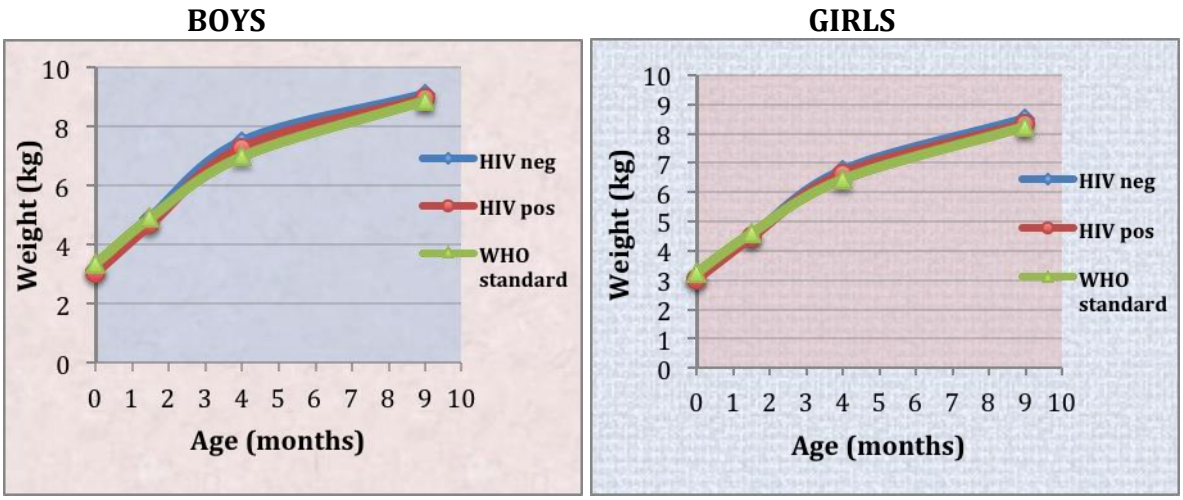
3.3 Head circumference

Table 3: Head circumference of boys and girls according to maternal HIV-status

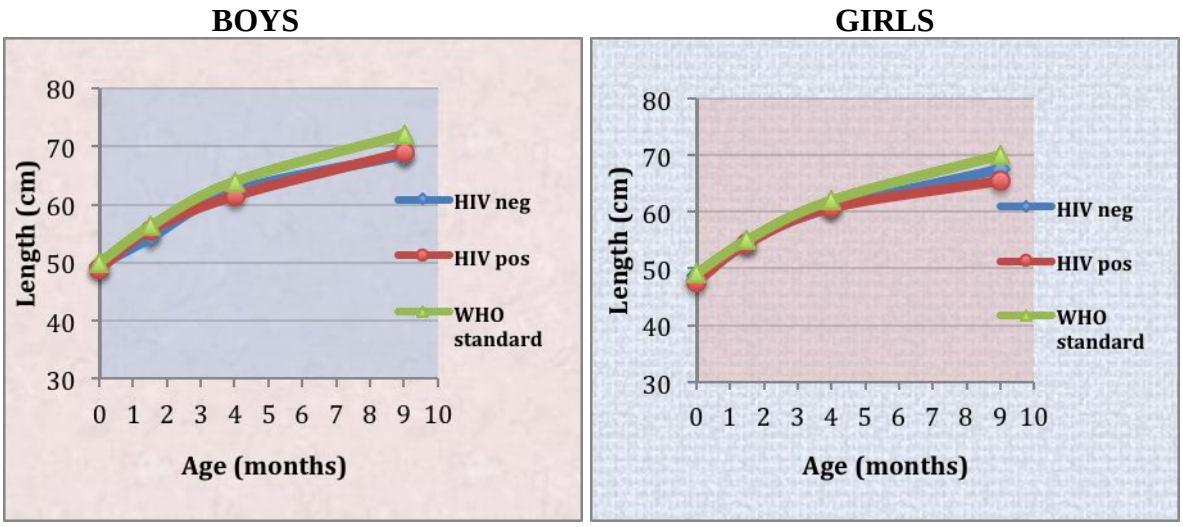
		Maternal HIV status	N	Mean head circumference (cm)	SD	p-value	95% CI lower	95% CI upper
BOYS	**Birth**	Neg	52	34,5	1,77	0,65	-0,65	1,03
		Pos	68	34,3	2,62			
	6 weeks	Neg	52	38,6	2,73	0,16	-2,71	0,45
		Pos	68	39,8	5,23			
	4 months	Neg	52	43,6	3,15	0,88	-1,51	1,29
		Pos	68	43,7	4,30			
	9 months	Neg	52	46,7	3,78	0,05	-0,01	2,27
		Pos	68	45,6	2,53			
GIRLS	**Birth**	Neg	62	34,2	1,27	0,07	-0,70	0,83
		Pos	62	34,1	2,74			
	6 weeks	Neg	62	38,1	2,28	0,17	-1,36	0,24
		Pos	62	38,7	2,20			
	4 months	Neg	62	43,5	4,94	0,04	0,08	2,97
		Pos	62	42,0	2,94			
	9 months	Neg	62	45,1	2,88	0,45	-2,09	0,93
		Pos	62	45,6	5,28			

Table 3 shows that boys born of HIV negative mothers (n = 52) had a tendency to higher mean head circumference at birth and 9 months, while girls born of HIV negative mothers (n = 62) had a tendency to higher mean head circumference at birth and 4 months. The differences however, were statistically significant only for the girls at the age of 4 months ($p < 0,05$), but these differences disappeared at 9 months of age ($p > 0,05$).

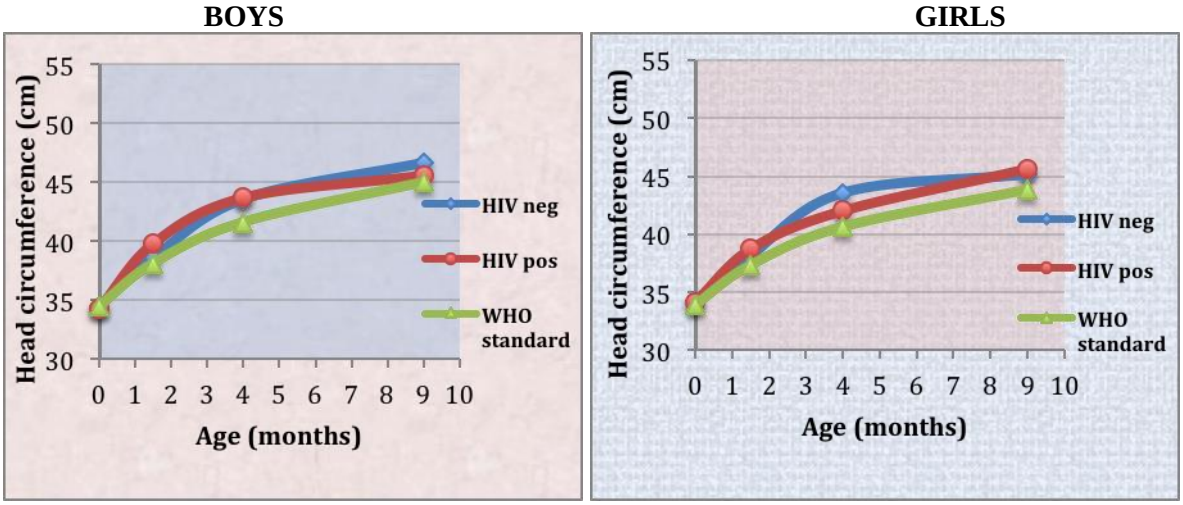
3.4 Growth curves according to maternal HIV-status and WHO´s growth standards



Curve 1: Weight of boys and girls according to maternal HIV status and WHO growth standard



Curve 2: Length of boys and girls according to maternal HIV status and WHO growth standards



Curve 3: Head circumference of infants according to maternal HIV status and WHO growth standards

3.5 Comparing growth percentiles with WHO´s growth standards

Previous comparing of weight, length and head circumference has shown no difference in the infants according to maternal HIV-status. In this part we have therefor decided to look at the group as one, and find out how many of the children fell beneath the 3rd percentile and above the 97th percentile for WHO´s growth standards.

Table 4: Percentage of infants who are beneath the 3rd and above the 97th percentile for WHO´s growth standards

		Weight (N_{boys} = 122, N_{girls} = 122)		Length (N_{boys} = 116, N_{girls} = 122)		Head circumference (N_{boys} = 120, N_{girls} =124)	
		< 3rd percentile (%)	> 97th percentile (%)	< 3rd percentile (%)	> 97th percentile (%)	< 3rd percentile (%)	> 97th percentile (%)
BOYS	Birth	4.9	0.8	15.5	6.9	16.7	9.2
	6 weeks	7.4	0.0	22.4	12.9	5.0	18.3
	4 months	6.6	13.1	20.7	6.9	0.8	40.8
	9 months	13.1	11.5	36.2	6.0	5.0	21.7
GIRLS	Birth	2.5	0.8	12.3	4.9	4.0	5.6
	6 weeks	4.0	3.3	22.1	15.6	0.8	23.4
	4 months	9.0	6.6	15.6	7.4	1.6	23.4
	9 months	4.9	6.6	37.7	9.0	6.5	27.4

Table 4 shows that a lot of the boys and girls fell either beneath the 3rd percentiles or above the 97th percentile for WHO´s growth standards. This is highly expressed especially for length, where 12.3% to 37.7% is beneath the 3rd percentile, and for head circumference, where 5.6 to 40.8% is above the 97th percentile at any time point. These differences are also reflected in the mean measurements in curve 2 and 3, showing that the mean for length lies lower and the mean for head circumference lies higher for the infants in comparison to the WHO growth standards. However it looks like the differences are less at birth. The differences for the weight percentiles are less expressed.

3.6 Low birth weight

Low birth weight is defined as weight at birth < 2500 g. (28) One of the criteria for inclusion was that all children should have registered their birth weight. When comparing low birth weight according to maternal HIV-status, we therefor used all 774 pairs of mothers and children. We have not separated between boys and girls in this part.

Table 5: Low birth weight (< 2500 g) of infants according to maternal HIV-status

	HIV negative		**HIV positive**	
	< 2500 g	**> 2500 g**	**< 2500 g**	**> 2500 g**
N	37	371	45	321
Percentage (%)	9.1	90.9	12.3	87.7

Table 5 shows that 12.3% of the children born of HIV positive mothers had a low birth weight. That is 3.2% more then the children born of HIV positive mothers, but our analysis show that this difference is not significant with a p-value = 0,145.

3.7 Other factors

When comparing other factors according to maternal HIV-status, we have used all data available in our study group of 774 pairs of mothers and children. Not all the information was available for all pairs.

Table 6: Others factors according to maternal HIV-status

		HIV negative		HIV positive	
		N	%	N	%
Age	< 20 years	127	31.2	51	13.9
	> 20 years	280	68.8	315	86.1
Education	≤ 7 years	75	18.4	81	22.1
	> 7 years	333	81.6	285	77.9
Marital status	Living alone	22	5.4	34	9.6
	Cohabiting	8	2.0	6	1.7
	Married	376	92.6	315	88.7
Breastfeeding	6 weeks	309	96.6	269	90.0
	4 months	192	98.5	198	83.5
	9 months	177	83.9	117	58.5
Follow-up visits with infant	< 3 visits	193	47.3	171	46.7
	≥ 3 visits	215	52.7	195	53.3
Deceased mothers	No	407	99.8	355	97.0
	Yes	1	0.2	11	3.0
Deceased infants	No	396	97.1	332	90.7
	Yes	12	2.9	34	9.3

HIV positive mothers were older (p = 0,00), had less education (though not significant, p = 0,18) and were more often single mothers (p = 0,02) compared with the HIV negative one. Fifteen times as many mothers in the HIV group had died (3.0 % versus 0.2%), a significant difference (p = 0,002). More than half of the children were having more than 3 follow-up visits in both groups.

A higher percentage of mothers were breastfeeding at all time points in the HIV negative group (p = 0,00) compared to the HIV positive group. A difference increasing from 6.6% 6 weeks postpartum to 25.4% 9 months postpartum.

There were 6.4% more deceased infants in the HIV positive group (p = 0,00); three times more compared to the HIV negative group.

4.0 DISCUSSION

We investigated 774 infants born to HIV positive and negative mothers. Surprisingly we found no significant difference between the two groups. In the following discussion we will focus upon bias in our method and results.

4.1 Method

Sources of bias

- *Selection of our study group:* The original study had a total of 1050 participating women. The total numbers of excluded files were 276, representing 26,3 % of the total group. This could represent a selection bias leading to an unreliable result. There can be many sources of bias when one compares those who were willing to participate in the study from the beginning, versus those who did not.
    1) The participating women may have had another health-seeking behaviour: been more conscious about attending the follow-up visits, been more conscious about their own and the baby´s health, had more knowledge and a different understanding of the importance of follow-up routines, and been higher educated.
    2) The data was only collected from the three peri urban clinics outside Harare and not from other parts of the country. The study population would therefor be a selective part of the population, and might not be representative for the total population.

- *Measurement of weight, length and head circumference:* The field activities were performed by trained midwives/nurses and laboratory people. The qualified personnel

team was trained for two weeks in study techniques, such as recruitment of the women, explanation of the study protocol, practical data collection etc. (27)
The measurements are probably representing many sources of bias, even when performed systematically. Even though it is described that the nurses and midwives were trained, we do not know if the measurements were standardized or not. There can be errors according to the accuracy of the measurements, such as weight scales in gram or kilogram, stretching of the baby´s legs when measuring the length and standard measure technique for head circumference? Different persons were doing the measures, which can lead to different measurements due to different techniques. In the original study, there are only described that anthropometrical measurements were taken at each visit, but no further details about the methods. (27) Further, we have no information about the equipment used at the three clinics. Were they using same types of weight scales and measurement tapes? If different weight scales and measurement tapes were used, it can have led to significant sources of error, and we do not know whether the scales were calibrated regularly or not. However it is likely to believe that these measurement errors were equally divided in both study groups, and therefore it is possible that our findings are true.

- *Gestational age:* The women were recruited in the study from gestational age 36, but we do not know which gestational age they gave birth, and therefore it is uncertain whether the HIV positive mothers gave birth to more prematurely babies. The more prematurely the infants are born, the more likely their weight and length is to be affected. And how sure was the determination of gestational age in the first place? If a lot of the age determinations were wrong, surely this could alter the actual values.

- *HIV-status:* A confirmatory HIV test was done on all women, regardless of their national HIV test result. The HIV results that were discrepant, false negative and false positive were retested using an ELISA-test. HIV-exposed children were screened for HIV using DNA-PCR up to 9 months of age. Cord blood was collected at birth, and venous blood was collected at the other visits, for HIV-DNA PCR analyses. (27)
HIV-DNA PCR analyses are the standardised tests used for children < 18 months of age. The test has a 55% sensitivity at birth, increasing to >90 % by 2 to 4 weeks of age and 100% at 3 and 6 months. The specificity is 99.8 % at birth and 100 % at 1, 3, and 6 months. (29)

In the original study, HIV positive mothers received a single dose of Nevirapine, 200 mg, to be taken at the onset of labour to reduce the risk of MTCT of HIV. Their infants received a single dose of Nevirapine, 1-2 mg, within 72 hours after delivery. How much did this reduce the number of infants born with HIV? And as a result of this, could that have affected the infants´ growth after birth? (27)

We did not have any information about the stage of the mothers´ HIV-disease. Could the stage of disease affect the intrauterine growth and thereby the birth measurements? If there were more women in an early HIV-stage, could this be the reason for no statistically significant difference in growth according to maternal HIV-status? Compared to WHO data, our data were pretty much similar at birth, which could indicate that these women were not heavily affected or that the care for these women was better than expected.

- *Attendance:* The follow-up consultations were scheduled at 6 weeks, 4 months and 9 months after birth. After a year, follow-up was every 6 months for 5 years.
  As can be seen from table 10, 52.7 % of the HIV negative and 53.3 % of the HIV positive mothers attended more than 3 visits during the follow-up period. Only a few attended all the follow-up visits during the 5 years. Different reasons for not showing up at all the follow-up visits could be: transport difficulties, residence far from the clinics, sudden illness, ”no need” for it because the child seemed well or forgot to meet.

- *Criteria of inclusion and exclusion:* We excluded the children with missing information about weight, length or head circumference at birth. We also excluded children without known gender and HIV-status and mothers without known HIV-status. We have not collected information that can say if there were any twins in our study population, and therefor we do not have exact numbers for this. Twins in general have a lower birth weight than single babies, but since we do not know how many there were in our study and how they were divided in the two groups, we do not know how this affect our results. But since twin births in general are low frequent, this is probably of no value

4.2 Results

There were no differences in growth according to maternal HIV status in our analysis.

Comparison of growth in the two groups

Our analyses showed no statistically significant difference in the children's growth according to maternal HIV-status (except for head circumference at 4 months of age for the girls). This could be due to the sources of bias discussed above or other reasons we will discuss below. There is also a possibility that the results we found are true, and that there were no differences in the two groups.

- *When analysing and comparing growth* we only used those children with measurements recorded at all time points. This means that we did not register those infants who died during the first 9 months of life. Our findings show a threefold higher child mortality among infants born by HIV positive mothers compared to HIV negative mothers. Since these were missed in our analysis and there was a higher mortality among children of HIV positive mothers, there is a possibility that this could have affected our results.

- *Other studies* show variable results. A study done in Burkina Faso in 1995-1996 showed no difference of significance at birth. This study included 956 pairs of mothers and their children. (30) In a study material from BHAMC, including 1045 mothers and their infants, there were significant lower birth weight and length in children born by HIV positive mothers, but no differences in birth head circumference. (31).

- *Health seeking behaviour:* It is possible that the women who knew that they were HIV positive and agreed to be a part of this study, were more conscious about their children´s health and diseases, and therefor took action earlier by seeking help from the health services, which could have improved their children´s growth.

- *Time spent on information giving and advises:* One can assume that HIV positive mothers received more thorough information and advices from health workers and the time spent on them were greater than for HIV negative women.

- *Information on infant feeding:* All women who were included in the study were informed about infant feeding. It is possible that HIV positive mothers in this study had a better knowledge about choosing the right nutrition for their children, than HIV positive mothers in general.

Low birth weight

We found that a higher proportion of children of HIV positive mothers had a low birth weight, a 3,2% difference. This difference was not significant. Because of possible measurement errors we cannot be sure if these results are reliable, but as described earlier, measurement errors were probably equally divided in both groups and as a result of this, our findings are still valuable. There might be a smaller or larger difference than the one we found. Unknown gestational week might also lead to possible errors.

Other factors

- *Age:* More of the women in the HIV positive group had an age > 20 years. It is uncertain if this is relevant for the child's growth.

- *Education:* HIV negative mothers had a higher education level, but these differences were minor. A higher education makes it easier to utilise information and advise given on child nutrition, and this could again affect children's growth. Even though differences according to maternal HIV status were low, it is possible that women who decided to join the study had a higher education than the population in general (including the HIV positive mothers); it could affect the nutrition given to their children, resulting in a better growth.

- *Marital status:* More HIV negative women were married, while more HIV positive mothers were living alone. The women who were married might have had a higher income because of economic support from their husbands, which could lead to more money to spend on food. Still this does not seem to have had big effects on our findings. It is likely to think that women living in a marital relationship have a lower prevalence of HIV because of a single sexual partner/stabile sexual behaviour.

- *Breastfeeding:* The HIV positive mothers breastfed less than the HIV negative mothers at all time points. Were the WHO guidelines followed in these cases? Did the children who were not breastfed receive proper supplement and did the HIV positive women receive ARV intervention? The HIV positive mothers received a single dose of Nevirapine at the onset of labour, and their children received a single dose within 72 hours after birth. This may have contributed to the fact that we did not find any statistical significant differences in growth between the to groups during the 9 months of follow-up. There is a possibility that true differences in growth would appear later. The data from the study period do not describe if the mothers and/or their infants received further essential treatment. No difference was found in child growth, but is it possible that children who were not breastfed could suffer from malnutrition, compared to those who were breastfed?

- *Follow-up visits with infant:* There were no difference in follow-up visits in the two groups, but in general we could say that the follow-up rate was low, which could have affected other findings in this study. This is also described under the discussion of methods.

- *Deceased mother:* As one could imagine, there were a higher proportion of deceased mothers in the HIV positive group. Could children of these mothers have a more affected growth? In that case, these children were lost in the follow-up, and thereby could have affected our results leading to a higher mean growth than the actual mean growth in the HIV positive mothers group. But since the numbers of deceased mothers were low, it is likely to think that this would marginally influence our results.

- *Deceased infant:* A higher proportion of children of HIV positive mothers died in this study. Half of the deceased children in this group were HIV positive them selves, which in turn could explain a big part of the differences according to maternal HIV status. And if we divide the children of HIV positive mothers in to two groups according to their child´s HIV status we find that 5.9% of HIV negative children deceased, compared to 22.1 % in the HIV positive children.

5.0 CONCLUSION

In our study we found no statistical significant differences in weight, length and head circumference according to maternal HIV-status the first 9 months of life for both genders. And neither did we find any significant differences in low birth weight. However these results may be questionable, because of a limited compliance on follow-up and uncertainty of measurements and skills of health workers. Still we believe our results are valuable since it is likely that measurement errors were equally divided, and that the follow-up frequency was similar in both the HIV positive and negative group. What we did find, was that HIV positive mothers had a higher mortality, and that the children of HIV positive mothers had a threefold higher mortality during the first 9 months of life. The child mortality differences in the two groups show that there is still a lot of work to be done to better the survival of children born of HIV positive mothers.

6.0 ACKNOWLEDGEMENTS

We would like to thank following people for their kind assistance:
Dr. Nyaradzai Edith Kurewa; Harare, Zimbabwe
Dr. Med Babill Stray-Pedersen; Professor in Gynaecology and Obstetrics, University of Oslo.

7.0 REFERENCES

1. Millennium Development Goals (MDGs)[Internet]. WHO 2013. [Quoted 28.01.13]. Accessible from http://www.who.int/topics/millennium_development_goals/about/en/index.html.
2. Hergum, H.P. Zimbabwe [Internet]. Store Norske Leksikon [Updated 28.06.12; Quoted 21.01.13]. Accessible from http://snl.no/Zimbabwe.
3. Williams, L. Background: Social conditions, People, Geography. I: Williams, L., red. Footprint Zimbabwe: Handbook. 1st edition. Bath: Footprint Handbooks Ltd; 2010. s. 248-250, 254.
4. Zimbabwe-næringsliv. [Internet]. Store Norske Leksikon. [Updated 15.01.13; Quoted 25.01.13]. Accessible from http://snl.no/Zimbabwe/næringsliv.
5. WHO Zimbabwe Statistics [Internet]. WHO; 2013. [Quoted 21.01.13]. Accessible from http://www.who.int/countries/zwe/en/.
6. UNICEF Zimbabwe Statistics [Internet]. UNICEF [Quoted 22.01.13]. Accessible from http://www.unicef.org/infobycountry/zimbabwe_statistics.html
7. PHR. Health in ruins: A man-made disaster in Zimbabwe, an emergency report [Internet]. Cambridge, Massachusetts; PHR; 2009. [Quoted 21.01.13]. Accessible from: http://physiciansforhumanrights.org/library/reports/zimbabwe-health-in-ruins-2009.html.
8. Human Development Reports [Internet]. UNDP; 2011 [Quoted 22.01.13] Accessible from http://hdr.undp.org/en/statistic/
9. UNAIDS World AIDS Day Report, 2012 [Internet]. Geneva. UNAIDS; 2012. [Quoted 23.01.13] Accessible from http://www.unaids.org/en/resources/publications/2012/name,76120,en.asp
10. Zimbabwe 2011 Country Operational Plan [Internet]. PEPFAR; 2011. [Quoted 23.01.11]. Accessible from http://www.pepfar.gov/countries/cop/c54518.htm
11. Quinn, T.C. The global human immunodeficiency virus pandemic [Internet]. Up To Date [Updated 07.01.13; Quoted 23.01.13] Accessible from http://www.uptodate.com/contents/the-global-human-immunodeficiency-virus-pandemic?source=search_result&search=hiv+zimbabwe&selectedTitle=2~150

12. Global HIV/AIDS Zimbabwe [Internet]. United States Centers for Disease Control and Prevention (CDC) [Updated 27.03.12; Quoted 23.01.13]. Accessible from http://www.cdc.gov/globalaids/Global-HIV-AIDS-at-CDC/countries/Zimbabwe/
13. WHO, UNAIDS and UNICEF. Epidemiological Fact Sheet on HIV and AIDS, Zimbabwe[Internet]. 2008 Update. Geneva: WHO; 18.02.2009[Quoted 24.01.13]. Accessible from: http://apps.who.int/globalatlas/predefinedReports/EFS2008/full/EFS2008_ZW.pdf
14. UNAIDS report on the global AIDS epidemic 2012 [Internet]. UNAIDS; 2012 [Quoted 22.01.13]. Accessible from http://www.unaids.org/en/resources/publications/2012/name,76121,en.asp
15. Fleming, A.F., McIntyre J.A. and Johnstone F.D. HIV-infections and AIDS in pregnancy: Transmission of HIV. I: Lawson J.B., Harrison K.A, Bergstrøm S.,red. Maternity care in developing countries. London: RCOG Press; 2001.p.339.
16. Gillespie, S.L. Epidemiology of pediatric HIV infection [Internet]. Up To Date. [Updated 16.03.12; Quoted 24.01.13]. Accessible from http://www.uptodate.com/contents/epidemiology-of-pediatric-hiv-infection?source=search_result&search=mtct+hiv&selectedTitle=1%7E150
17. Willoughby, A. Mother-to-child Transmission of HIV: Risk factors. I: Essex, M., Mboup, S., Kanki, P.J., Marlink, R.G. and Tlou, S.D., red. Aids in Africa. 2nd edition. New York: Kluwer Academic/Plenum Publishers; 2002. P.253-254.
18. Moëll, C. and Hagenäs, L. Barnets normal tillväkst och utveckling: Normal utveckling av längd och vikt. I: Moëll, C. and Gustafsson, J., red. Ped. 1st edition. Stockholm: Liber; 2011. P.17-20 and p.46-48.
19. Boom, J.A. Normal growth patterns in infants and prepubertal children [Internet]. Up To Date. [Updated 19.06.12; Quoted 24.01.13]. Accessible from http://www.uptodate.com/contents/normal-growth-patterns-in-infants-and-prepubertal-children?source=search_result&search=infant+growth&selectedTitle=1%7E150
20. WHO WHO Child Growth Standards [Internet]. WHO; 2009 [Quoted 22.01.13]. Accessible from http://www.who.int/childgrowth/standards/velocity/technical_report/en/index.html
21. WHO Guidelines on HIV and infant feeding 2010 [Internet]. WHO; 2010 [Quoted 28.01.13]. Accessible from

http://www.who.int/maternal_child_adolescent/documents/9789241599535/en/index.html

22. Hergum, H.P. Harare [Internet]. Store Norske Leksikon [Updated 14.09.09; Quoted 16.09.12]. Accessible from http://snl.no/Harare
23. Chitungwiza [Internet]. Wikipedia [Updated 08.07.12; Quoted 16.09.12]. Accessible from http://en.wikipedia.org/wiki/Chitungwiza
24. Mashonaland East [Internet]. Wikipedia [Updated 10.09.12; Quoted 16.09.12]. Accessible from http://no.wikipedia.org/wiki/Mashonaland_East
25. UNAIDS. HIV estimates with uncertainty bounds 1990-2011 [Internet] UNAIDS; 2012 [Quoted 21.01.13]. Accessible from: http://www.unaids.org/en/resources/campaigns/20121120_globalreport2012/globalreport/
26. Stray-Pedersen, B. Babill Stray-Pedersen Web Portal [Internet]. Oslo: Faculty of Medicine, University of Oslo; 2009[Quoted 28.01.13]. Accessible from: http://www.babill.no/
27. Kurewa, N.E. PMTCT of HIV: Realities and challenges of following up mother and child pairs over five years in Zimbabwe [PhD]. Oslo: Faculty of Medicine, University of Oslo; 2010.
28. WHO. Health status statistics: Morbidity [Internet]. WHO [Quoted 01.02.13] Accessible from http://www.who.int/healthinfo/statistics/indlowbirthweight/en/index.html
29. Schwarzwald, H. Diagnostic testing for HIV infection in infants and children younger than 18 months [Internet]. UpToDate [Updated 04.12.12; Quoted 31.01.13]. Accessible from: http://www.uptodate.com/contents/diagnostic-testing-for-hiv-infection-in-infants-and-children-younger-than-18-months?source=search_result&search=HIV+testing+of+infants&selectedTitle=2~108
30. Sombié I, Nacro B, Tiendrébéogo S, Dao B, Cartoux M, Meda N, Ky-Zerbo O, Dabis F, Mandelbrot L, Van de Perre P. [Maternal HIV infection and the anthropometric characteristics of children at birth in Burkina Faso. DITRAME Study Group]. Sante. 1999 May-Jun;9(3):173-7
31. Kurewa EN, Gumbo FZ, Munjoma MW, Mapingure MP, Chirenje MZ, Rusakaniko S, Stray-Pedersen B. Effect of maternal HIV status on infant mortality: evidence from a 9-month follow-up of mothers and their infants in Zimbabwe. J Perinatol. 2010

Feb;30(2):88-92